

A Comparison of Energy Instruments and Stapling Devices to Dissect Intersegmental Planes in Segmentectomy: A Randomized Controlled Trial

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Objectives

Because of the common use of low-dose computed tomography (CT) and other means of examination, there is an increasing number of patients diagnosed with small pulmonary nodules. Anatomical segmentectomy has been one of the standard surgical treatments for these patients. The two main approaches in dissection of the intersegmental plane involve a stapling device and energy instrument separation. Our study will compare the perioperative outcomes of these two approaches. The primary outcome will be the percentages of postoperative complications. The secondary outcomes will be preoperative and postoperative lung function, duration of surgery, blood loss during surgery, postoperative hospital stay, and the duration of drainage.

Background

Lung cancer is one of the most serious life-threatening diseases. It has the highest worldwide morbidity and mortality among all malignant tumors [1]. Because of the frequent use of low-dose CT and other means of examination [2], an increasing number of patients with lung cancer are detected in the early phase of the disease. Anatomical segmentectomy is one of the standard surgical procedures [3] for small pulmonary nodules or ground glass opacities (GGOs), which are highly suspect or pathologically confirmed as early lung cancer lesions.

Dissection of the intersegmental plane during segmentectomy is challenging for thoracic surgeons because of complicated anatomical relationships and variations and the lack of a boundary between pulmonary segments. There are two main approaches in the dissection of the intersegmental plane [4][5] that involve stapling devices and an energy instrument separation. However, only a few retrospective studies have reported the perioperative outcomes of these two approaches in traditional segmentectomy and robot-assisted segmentectomy.

Yoshikazu Miyasaka and his colleagues [6] conducted a retrospective study of 49 patients who underwent segmentectomy of the lung in 2010. The intersegmental plane was divided with only a mechanical stapler in 18 patients, and electrocautery was used in the other 31 patients. There was no significant relationship between the methods of making intersegmental planes and postoperative complications and/or lung functions. Takashi Ohtsuka et al. [7] analyzed 47 patients who underwent segmentectomy in 2012. Twenty-two patients underwent intersegmental plane dissection with electrocautery alone, and 25 patients underwent intersegmental plane dissection in combination with electrocautery and staplers. There was no statistical difference between the electrocautery alone group compared with the group treated with a combination of electrocautery and staplers in the duration of surgery (282 vs. 290 minutes), intraoperative blood loss (203 vs. 151 mL), duration of chest tube placement (3.2 vs. 3.1 days), postoperative hospital stay (11.0 vs. 10.0 days), postoperative loss of forced expiratory volume during the first second (13 vs. 8%), loss of forced vital capacity (11 vs. 6%), or incidence of minor postoperative complications [9% (2/22) vs. 16% (4/25); $p = 0.30$]. However, the incidence of prolonged air leaks was higher in the electrocautery alone group than in the group treated with a combination of electrocautery and staplers [14% (3/22) vs. 4% (1/25); $p = 0.025$]. The cost of materials for sealing the air leaks was €964 per patient in the electrocautery alone group and €1,594 per patient in the group treated with a combination of electrocautery and staplers. Hiroyuki Tao [8] also performed a retrospective study on lung function in 2016. The intersegmental planes were divided by either electrocautery or

with a stapler in 22 patients and with a stapler alone in 19 patients. There was no correlation between the actual/predicted ratio of remnant lung volume and pulmonary function based on the method of division.

As previously mentioned, there has been no definitive conclusion about which method is better. We expect the use of a stapling device will result in less perioperative complications but will have disadvantages in the reservation of lung functions and medical costs. To compare the feasibility, safety, and economic efficiency between these two methods, we plan to conduct a prospective study.

References

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Research Strategy

We propose to conduct a prospective, single-center, single-blind, randomized, controlled trial.

Inclusion Criteria:

1. Age: 18–70 years of age

2. Pulmonary nodules or GGO found in chest CT examinations that conform with indications for segmentectomy mentioned in the National Comprehensive Cancer Network guidelines:

(1) Poor pulmonary reserve or other major comorbidity that contraindicates lobectomy;

(2) Peripheral nodule ≤ 2 cm with at least one of the following:

1) Pure adenocarcinoma *in situ* histology;

2) Nodule has $\geq 50\%$ ground-glass appearance on CT;

3) Radiologic surveillance confirms a long doubling time (≥ 400 days).

3. Normal preoperative tests, such as routine blood examinations, liver function, renal function, and coagulation function.

4. American Society of Anesthesiologists score: Grades I–III

5. Patients coordinated with treatment and research and who provide informed consent

Exclusion Criteria:

1. Patients with a history of a malignant tumor or who have accepted neoadjuvant chemotherapy and/or radiotherapy

2. Patients with comorbidities in the cardiovascular, kidney, lung, or hematopoietic system who cannot tolerate the surgery

3. Psychiatric patients

4. Patient who have a history of chest trauma or surgery in the ipsilateral chest.

Case Load:

We will set the incidence percentage of postoperative complications as our primary endpoint. According to our calculations, a total of 136 patients will be enrolled (each group will be comprised of 68 patients). Based on our previous clinical observations and current reports, a sample size of 62 participants per group is estimated to provide a 90% power to detect a between-group difference of 10% incidence percentage of postoperative complications in the stapling device group and 33% in the energy instrument group, with a two-sided significance level of 5%. To compensate for a 10% loss to follow-up in the prespecified subgroup analyses, the sample size will be increased to 68 participants in each group.

Surgical Procedures:

All enrolled patients will be treated with robot-assisted segmentectomy. After removing the relevant segmental arteries, veins, and bronchus, the lung will be fully inflated. The border of the segment will appear after recollapse of the lung, because the targeted segment should remain inflated. We will use the da Vinci monopolar cautery hook or da Vinci Harmonic™ ACE, or Endo GIA™ or Echelon™ auto-suture single use stapler and single use reload device to dissect the intersegmental plane along the determined border. If fast-frozen pathology confirms lung cancer, we will perform a lymphadenectomy. Finally, a drainage tube will be inserted.

Primary Endpoints:

The incidence percentage of postoperative complications, including air leakage, atelectasis, hemorrhage, pulmonary infection, and pulmonary embolism

Secondary Endpoints:

1. The incidence percentage of each postoperative complication (especially air leakage, which will be quantified by the Medela Thopaz™ digital quantitative chest drainage system)
2. Preoperative lung function, postoperative lung function on the 3rd day and 1st month after surgery
3. Postoperative hospital stay, postoperative intensive care unit stay, duration of drainage, and mortality at 30 days after surgery
4. The duration of surgery, blood loss during surgery, and the percentage of conversion to open surgery
5. Tumor location, pathological results, number of dissected lymph nodes, and the TMN stage
6. Medical costs (including total medical costs and the cost of materials)

Statistical Analysis:

An independent data monitoring committee (DMC) reviewed data from the study after 35 and 70 participants were recruited. The results of these interim checks were known only to the data manager and DMC. The trial was stopped early by the DMC due to a marked difference between groups after recruiting 70 patients.

Analysis was performed on an intention-to-treat basis. All analyses were performed using SPSS software (version 23; IBM SPSS, Chicago, IL, USA). Primary outcome analysis was performed by a simple categorical frequency comparison using a χ -square test. Secondary outcome analyses included unpaired Student's *t* tests for duration of surgery, duration of drainage, postoperative hospital stay, lung function, and medical costs; Mann-Whitney *U* tests for blood loss during surgery and postoperative ICU stay; and χ -square tests for the percentage of conversion to open surgery and mortality at 30 days after surgery. Sensitivity analysis of the primary outcome using logistic regression was undertaken to adjust for gender, age, smoking, tumor location, approach (robotic or VATS), and method of dissecting intersegmental planes (stapling device or energy instrument).